



Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

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Invasive Mycoses

Introduction (Last updated December 22, 2015; last reviewed December 22, 2015)

The fungal infections to be discussed in this section include cryptococcosis, histoplasmosis, and coccidioidomycosis. Candidiasis and pneumocystosis are discussed in other sections of this document. Blastomycosis, penicilliosis, and paracoccidioidomycosis are not discussed because their current incidence as opportunistic infections among patients with HIV-1 infection in the United States is very low. In addition, aspergillosis is no longer addressed in these guidelines because of the low incidence of this mycosis among HIV-infected persons without other underlying risk factors and the management of aspergillosis is otherwise similar to that in persons with other immunodeficiencies.

Cryptococcosis (Last updated September 17, 2015; last reviewed September 17, 2015)

Epidemiology

Most HIV-associated cryptococcal infections are caused by *Cryptococcus neoformans*, but occasionally *Cryptococcus gattii* is the etiology. *C. neoformans* is found worldwide, whereas *C. gattii* most often is found in Australia and similar subtropical regions and in the Pacific Northwest. Before the era of effective antiretroviral therapy (ART), approximately 5% to 8% of HIV-infected patients in developed countries were diagnosed with disseminated cryptococcosis.¹ Current estimates indicate that every year, nearly 1 million cases of cryptococcal meningitis are diagnosed worldwide and the disease accounts for more than 600,000 deaths.² With the availability of effective ART, the incidence has declined substantially in areas with ART access, and most new infections are being recognized in patients recently diagnosed with HIV infection.³ Most cases are observed in patients who have CD4 T lymphocyte (CD4) cell counts <100 cells/ μ L.

Clinical Manifestations

In HIV-infected patients, cryptococcosis commonly presents as a subacute meningitis or meningoencephalitis with fever, malaise, and headache.¹ Classic meningeal symptoms and signs, such as neck stiffness and photophobia, occur in only one-quarter to one-third of patients. Some patients experience encephalopathic symptoms, such as lethargy, altered mentation, personality changes, and memory loss that are usually a result of increased intracranial pressure.

Cryptococcosis usually is disseminated when diagnosed in an HIV-infected patient. Any organ of the body can be involved, and skin lesions may show myriad different manifestations, including umbilicated skin lesions mimicking molluscum contagiosum. Isolated pulmonary infection is also possible; symptoms and signs include cough and dyspnea in association with an abnormal chest radiograph, which typically demonstrates lobar consolidation, although nodular infiltrates have been reported. Pulmonary cryptococcosis may present as acute respiratory distress syndrome and mimic *Pneumocystis* pneumonia.

Diagnosis

Analysis of cerebrospinal fluid (CSF) generally demonstrates mildly elevated levels of serum protein, low-to-normal glucose concentrations, and pleocytosis consisting mostly of lymphocytes. Some HIV-infected patients will have very few CSF inflammatory cells, but a Gram's stain preparation, or an India ink preparation if available, may demonstrate numerous yeast forms. The opening pressure in the CSF may be elevated, with pressures ≥ 25 cm H₂O occurring in 60% to 80% of patients.^{4,5}

Cryptococcal disease can be diagnosed through culture, CSF microscopy, or by cryptococcal antigen (CrAg) detection. In patients with HIV-related cryptococcal meningitis, 55% of blood cultures and 95% of CSF cultures